In the Specification:

At page 1, in the first sentence following the title, after "This patent application" please insert the text -- is a continuation application of U.S. Patent Application Serial No. 09/061,400, filed on April 16, 1998 (allowed), which in turn --

At page 7, line 15, please replace "12301 Parklawn Drive, Rockville, MD 20852" with -- 10801 University Boulevard Manassas, VA 20110-2209--.

In the Claims:

Please cancel claims 1-47, 49-50, 52-75 and 78-79 without prejudice.

Please add new claims 80-114 as follows:

80. An isolated nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID No: 1;

(b) an isolated nucleic acid molecule comprising the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number 98409;

(c) an isolated nucleic acid molecule which is a unique fragment of the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1;

(d) at least 50% identical to the nucleotide sequence of SEQ ID No: 1;

(e) an isolated nucleic acid molecule that hybridizes under stringent conditions to the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1;

(f) an isolated nucleic acid molecule which is a degenerate sequence variant of the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1;

(g) an isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID No: 2;

(h) an isolated nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence which is at least 75% identical to the polypeptide having the amino acid sequence of SEQ ID No: 2; and

(i) an isolated nucleic acid molecules which is complementary to the nucleic acid molecule in any of subparts (a), (b) or (e).

81. An oligonucleotide selected from the group consisting of:

(a) an oligonucleotide that hybridizes to a unique fragment of the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1;

(b) an oligonucleotide that hybridizes to a unique fragment of the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1 under stringent conditions;

(c) an oligonucleotide that hybridizes to a unique fragment of the nucleic acid molecule having the nucleotide sequence of SEQ ID No: 1 under intracellular conditions;

(d) an oligonucleotide as in subpart (a) comprising at least one modification in a nucleotide base, backbone sugar, phosphate or sugar-phosphate linkage;

(e) an oligonucleotide as in subpart (a) comprising a peptide nucleic acid backbone;

(f) an oligonucleotide as in subpart (a) which is detectably labeled;

(g) an oligonucleotide as in subpart (a) which is biotinylated, radiolabeled or fluorophore-conjugated;

(h) an oligonucleotide as in subpart (a) wherein said unique fragment is at least 9 nucleotides in length;

(i) an oligonucleotide as in subpart (a) wherein said unique fragment is at least 15 nucleotides in length;

(j) an oligonucleotide as in subpart (a) wherein said unique fragment is at least 21 nucleotides in length;

(k) an oligonucleotide as in subpart (a) wherein said unique fragment is a locus comprising a 5' untranslated sequence, transcription initiation site, coding sequence, intron-exon boundary, polyadenylation site, or 3' untranslated sequence in the nucleic acid of SEQ ID No: 1; and

(l) an oligonucleotide having a nucleotide sequence selected from the group consisting of SEQ ID Nos: 4, 5, 6, 7 and 8.

82. An antisense vector comprising the oligonucleotide of claim 81.

83. An antisense pharmaceutical composition comprising the oligonucleotide of claim 81 or a vector of comprising said oligonucleotide, dispersed in a pharmaceutically acceptable vehicle.

84. An isolated MRP-β polypeptide selected from the group consisting of:

(a) a polypeptide comprising the amino acid sequence of SEQ ID No: 2;

(b) a polypeptide comprising an amino acid sequence sharing at least 75% sequence identity with the amino acid sequence of SEQ ID No: 2;

(c) a polypeptide which is an epitope unique to the MRP-β polypeptide having the amino acid sequence of SEQ ID No: 2; and

(d) the polypeptide as set forth in subpart (c), where said epitope is displayed by a cell expressing an MRP-β gene.

85. An antibody that binds selectively to the polypeptide of claim 84, or an antigen-binding fragment thereof.

86. A fusion polypeptide selected from the group consisting of:

(a) a fusion polypeptide comprising an antigen-binding fragment of claim 85.

(b) a fusion polypeptide as set forth in subpart (a) further comprising a cytotoxic polypeptide, such that said fusion polypeptide stimulates cytolysis of a cell expressing an MRP-β gene; and

(c) a fusion polypeptide as set forth in subpart (a) further comprising a chemoattractant, such that said fusion polypeptide stimulates destruction of a cell expressing an MRP-β gene by macrophages, killer T cells or cytotoxic T cells.

87. An expression vector comprising a nucleic acid molecule encoding the polypeptide of claim 84.

88. A cell selected from the group consisting of:

(a) a cell transfected with the expression vector of claim 87;

(b) a cell transfected with the expression vector of claim 87, wherein said cell is immortalized under cell culture conditions;

(c) a cell as in subpart (b), wherein said cell is of human origin;

(d) a cell as in subpart (b), wherein said cell is a unicellular organism;

(e) a cell as in subpart (d), wherein said cell is yeast cell; and

(f) a cell as in subpart (a), wherein said cell is a non-human mammalian embryonic blastocyst cell.

89. A non-human mammal produced by intrauterine implantation of a blastocyst comprising a cell transfected with an expression vector comprising a nucleic acid molecule encoding the polypeptide of claim 84, wherein said cell is a non-human mammalian embryonic blastocyst cell.

90. A progeny of the mammal of claim 89, said progeny characterized by germline integration of said nucleic acid encoding said polypeptide.

91. A null vector comprising nucleic acid encoding a non-expressible variant of a polypeptide having an amino acid sequence sharing at least 75% sequence identity with the amino acid sequence of SEQ ID No: 2

92. A cell transfected with the null vector of claim 91.

93. The cell of claim 92, wherein said cell is a non-human mammalian embryonic blastocyst cell.

94. A non-human mammal produced by intrauterine implantation of a blastocyst comprising the cell of claim 93.

95. A progeny of the mammal of claim 94, said progeny characterized by germline integration of said nucleic acid molecule.

96. A method of detecting expression of an MRP-β gene, comprising the steps of:

(a) obtaining cellular tissue from a mammal suspected of harboring cells expressing an MRP-β gene encoding a polypeptide comprising the amino acid sequence of SEQ ID No: 2;

(b) releasing RNA from said cellular tissue;

(c) combining, under hybridization conditions, said released RNA with an oligonucleotide that hybridizes to the complement of SEQ ID No: 1 or a unique fragment thereof; and

(d) assaying said released RNA for formation of a hybrid comprising said oligonucleotide, formation of which indicates that cells of said tissue express said MRP-β gene.

97. The method of claim 48 or 96, wherein said cellular tissue is suspected of comprising transformed cells.

98. The method of claim 48, 51 or 96, wherein said oligonucleotide comprises a peptide nucleic acid backbone.

99. A method of characterizing drug-resistant phenotype of a transformed cell of mammalian origin, comprising the steps of:

(a) obtaining cellular tissue from a mammal suspected of harboring transformed cells;

(b) contacting said tissue with an antibody of claim 85, under conditions such that, if cells of said tissue display said an epitope selectively bound by said antibody, an antibody-epitope complex forms; and,

(c) assaying said tissue for the presence of said complex, formation of which indicates presence of transformed cells having a drug-resistant phenotype in said mammal.

100. The method of claim 51 or 99 wherein said cellular tissue is selected form the group consisting of:

(a) cellular tissue which is of mammary, respiratory tract, urogenital tract, endocrine system or immune system origin;

(b) cellular tissue which is of mammary origin and comprises a breast biopsy sample;

(c) cellular tissue which is of respiratory tract origin and comprises a bronchoalveolar lavage sample;

(d) cellular tissue which is of urogenital tract origin and comprises an ovarian, uterine or cervical biopsy sample;

(e) cellular tissue which is of urogenital tract origin and comprises a prostate or testicular biopsy sample;

(f) cellular tissue which is of endocrine system origin and comprises a pancreatic biopsy sample; and

(g) cellular tissue which is of immune system origin and comprises a spleen, bone marrow or lymph node biopsy sample.

101. A method of mitigating aberrant expression of an MRP-β gene, comprising administering an antisense pharmaceutical composition of claim 83 to a mammal suffering from effects of said aberrant expression, under conditions sufficient to attenuate a phenotype associated therewith.

102. A method of mitigating aberrant activity of an MRP-β gene, comprising administering an antisense pharmaceutical composition of claim 83 to a mammal suffering from effects of said aberrant activity, under conditions sufficient to attenuate a phenotype associated therewith.

103. A method of improving effectiveness of chemotherapy for a mammal afflicted with a multidrug-resistant tumor, comprising administering a chemotherapeutic drug to said mammal; and coadministering an antisense pharmaceutical composition of claim 83, such that said antisense pharmaceutical composition mitigates resistance of said tumor to said chemotherapeutic drug.

104. A method of treating a mammal suffering from aberrant expression of an MRP-β gene or a mammal suffering from aberrant activity of an MRP-β, comprising administering a

fusion polypeptide of claim 86 to said mammal, in an amount effective for destroying cells aberrantly displaying an epitope unique to an MRP-β polypeptide.

105. A method of treating a mammal afflicted with a multidrug-resistant tumor, comprising the step of administering a fusion polypeptide of claim 86 to said mammal, in an amount effective for destroying tumor cells displaying an epitope unique to an MRP-β polypeptide.

106. A method of identifying a modulator of MRP-β, comprising the steps of:

(a) contacting a cell transfected with a vector comprising a nucleic acid molecule encoding the polypeptide of claim 84 with a candidate modulator of MRP-β;

(b) assaying the level of MRP-β gene expression or MRP-β polypeptide expression in said cell, wherein a detectable fluctuation in said level indicates that said candidate is an MRP-β modulator.

107. A method of identifying a modulator of MRP-β, comprising the steps of:

(a) contacting a cell transfected with a vector comprising a nucleic acid molecule encoding the polypeptide of claim 84 with a substrate transported by MRP-β;

(b) contacting said cell with a candidate modulator of MRP-β;

(c) assaying the amount of said substrate exported by said cell, wherein a detectable fluctuation in said amount indicates that said candidate is an MRP-β modulator.

108. A method of identifying a modulator of MRP-β, comprising the steps of:

(a) contacting a cell transfected with a vector comprising a nucleic acid molecule encoding the polypeptide of claim 84 with a cytotoxin exported or sequestered by MRP-β;

(b) contacting said cell with a candidate modulator of MRP-β;

(c) assaying survival of said cell, a detectable fluctuation in which indicates that said candidate is an MRP-β modulator.

109. A method of identifying a modulator of MRP-β, comprising the steps of:

(a) contacting a cell transfected with a vector comprising a nucleic acid molecule encoding the polypeptide of claim 84 with a cytotoxin exported by MRP-β;

(b) contacting said with a candidate modulator of MRP-β;

(c) assaying efflux of said cytotoxin from said cell, a fluctuation in which indicates that said candidate is an MRP-β modulator.

110. An MRP-β modulator identified by the method of claim 106, 107, 108 or 109.

111. An MRP-β modulator of claim 110, wherein said modulator is an inhibitor or a small molecule.

112. A multidrug-resistance attenuating pharmaceutical composition comprising an MRP-β modulator dispersed in a pharmaceutically acceptable vehicle.

113. A method of improving effectiveness of chemotherapy for a mammal afflicted with a multidrug-resistant tumor, comprising the steps of:

(a) administering a chemotherapeutic drug to said mammal; and,

(b) coadministering a pharmaceutical composition of claim 112,

such that said composition mitigates resistance of said tumor to said chemotherapeutic drug.

114. The method of claim 113 wherein said tumor is of mammary, respiratory tract, urogenital tract, endocrine system of immune system origin.

REMARKS

The specification has been amended to recite the date of deposit and the current address of the ATCC depository.

Claims 1-79 were previously pending in the present application. Claims 1-47, 49-50, 52-75 and 78-79 have been cancelled without prejudice to further prosecution in this or another